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Re-evaluation Decision RVD2013-02

Ethylene Oxide

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Re-evaluation Decision

After a re-evaluation of the fumigant ethylene oxide, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act*, is granting continued registration of products containing ethylene oxide for sale and use in Canada.

The regulatory approach for the re-evaluation of ethylene oxide was first presented in the Proposed Re-evaluation Decision PRVD2010-21, *Ethylene Oxide*, a consultation document.[1] This Re-evaluation Decision[2] describes this stage of PMRA's regulatory process for the re-evaluation of ethylene oxide as well as summarizes the Agency's decision and the reasons for it.

Comments received during the consultation period were taken into consideration. These resulted in changes in the regulatory decision that was proposed in PRVD2010-21. Appendix I summarizes the comments received during the consultation period and provides the PMRA's response to these comments. Appendix II describes data requirements. Appendix III outlines the revised label statements.

The PMRA is aware that the United States Environmental Protection Agency (USEPA) carcinogenicity assessment of ethylene oxide is ongoing. Therefore, the status of ethylene oxide as a pest control product in Canada may be revised pending the outcome of the USEPA carcinogenicity assessment.

What Does Health Canada Consider When Making a Re-evaluation Decision?

The PMRA's pesticide re-evaluation program considers potential risks, as well as value, of pesticide products to ensure they meet modern standards established to protect human health and the environment. Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, presents the details of the re-evaluation activities and program structure.

Ethylene oxide has been re-evaluated under Re-evaluation Program 1. This program relies as much as possible on foreign reviews, typically the USEPA Reregistration Eligibility Decision documents. For products to be re-evaluated under Program 1, the foreign review must meet the following conditions:

- it covers the main science areas, such as human health and the environment, that are necessary for Canadian regulatory decisions;
- it addresses the active ingredient and the main formulation types registered in Canada; and
- it is relevant to registered Canadian uses.

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1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

The USEPA re-evaluated ethylene oxide and published its conclusions in a Tolerance Reassessment Progress and Risk Management Decision in 2006 and a Reregistration Eligibility Decision in 2008. The USEPA concluded that ethylene oxide was eligible for re-registration provided that risk-reduction measures were adopted. Further, the USEPA is currently evaluating ethylene oxide's carcinogenicity classification and will determine whether additional actions are warranted in the future.

Based on the outcome of the review of the USEPA, the PMRA has made a regulatory decision and requires appropriate risk-reduction measures for Canadian uses of ethylene oxide. In this decision, the PMRA took into account the Canadian use pattern and policies (for example, the federal Toxic Substances Management Policy).

The PMRA requires that mitigation measures be implemented to further protect workers and environment. In the long-term, the PMRA is proposing to work with registrants and stakeholders to develop and implement a guidance document on Fumigation Management Plans. It is also recommended that the registrant and/or users work towards improving the technologies to further reduce human exposure.

For more details on the information presented in this Re-evaluation Decision, please refer to the Science Evaluation in the related Proposed Re-evaluation Decision PRVD2010-21, *Ethylene Oxide*.

What Is Ethylene Oxide?

Ethylene oxide is a fumigant gas registered in Canada to control microorganisms. It is applied indoors using specialized chambers that are designed for use with ethylene oxide. The application rates and methods vary depending on the type and quantity of material to be treated, how the material is packed, the types of organisms to be killed, as well as the chamber size, temperature and relative humidity.

Currently, ethylene oxide is registered for use on whole or ground spices and processed natural seasonings (except mixtures containing salt) to control bacteria, and is regulated under the *Pest Control Products Act*. It is also approved as a food additive for fumigation of whole and ground spices under Division 16 of the Food and Drug Regulations. Finally, under the authority of Canada's *Food and Drugs Act*, it is used to sterilize medical and laboratory equipment, pharmaceuticals, cosmetics and aseptic packaging. The present Re-evaluation Decision only addresses the uses of ethylene oxide as a pest control product under the *Pest Control Products Act*.

Health Considerations

Can Approved Uses of Ethylene Oxide Affect Human Health?

Ethylene oxide is unlikely to affect your health when used according to the revised label directions.

People could be exposed to ethylene oxide or its reaction products (for example, ethylene chlorohydrin or ethylene glycol) by working in fumigation facilities or by consuming treated food. The PMRA considers two key factors when assessing health risks: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

The USEPA concluded that ethylene oxide may have potential human health risks of concern from occupational exposure, and additional risk-reduction measures were required. The USEPA also concluded that ethylene oxide or its reaction products were unlikely to affect human health as a result of food consumption, provided additional label amendments were adopted. These conclusions apply to the Canadian situation and the equivalent risk-reduction measures are required for Canadian products containing ethylene oxide.

Maximum Residue Limits

The *Food and Drugs Act* prohibits the sale of adulterated food; that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in or on certain foods. Food containing a pesticide residue that is at or below the established MRL does not pose an unacceptable health risk.

Ethylene oxide is currently registered in Canada for use on whole and ground spices and processed natural seasonings (except mixtures containing salt) and could be used in other countries on spices and natural seasonings that are imported into Canada. No specific MRLs have been established for ethylene oxide in Canada. Where no specific MRL has been established, a default MRL of 0.1 ppm, regulated under subsection B.15.002(1) of the Food and Drug Regulations, applies, which means that pesticide residues in a food commodity must not exceed 0.1 ppm. However, ethylene oxide is approved as a food additive under Division 16 of the Food and Drug Regulations, and may be used as a fumigant on whole or ground spices (excluding those containing salt) at levels consistent with Good Manufacturing Practices.[3] The food additive table stipulates an MRL of 1500 ppm for the reaction product ethylene chlorohydrin. This MRL was not modified during the course of the re-evaluation.

Environmental Considerations

What Happens When Ethylene Oxide Is Introduced Into the Environment?

Ethylene Oxide is unlikely to affect non-target organisms when used according to the revised label directions.

As ethylene oxide is used indoors and in vacuum or gas-tight chambers, the potential for environmental exposure is considered to be minimal. The PMRA concluded that the use of ethylene oxide as a pesticide is unlikely to cause harm to the environment. Standard environmental advisory label statements to minimize surface water contamination are required.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human health and environment. These directions must be followed by law. As a result of the re-evaluation of ethylene oxide, the PMRA is requiring further risk-reduction measures.

- Safety and awareness training for all employees in the fumigation facility.
- Fumigation only to be performed in vacuum or gas-tight chambers.
- Additional personal protective equipment for handlers.
- A reduction of the maximum application rate on spices and natural seasonings.
- Prohibition of the use in/on basil.
- Additional advisory and precautionary statements.
- Remove the claim for control of insects since the registrant does not support this claim.

[3] "Good Manufacturing Practice" is defined in the Food and Drug Regulations (B.01.044) as: "where the limit prescribed for a food additive in a Table to section B.16.001 is stated to be "Good Manufacturing Practice", the amount of the food additive added to a food in manufacturing and processing shall not exceed the amount required to accomplish the purpose for which the additive is permitted to be added to that food."

Additional Considerations

Following the publication of the PRVD2010-21, the PMRA identified that some American food and drug regulations are cited on the current registered label. Those regulations must be removed from the label as they do not apply to Canada. Statements and instructions that are not related to pesticidal use must also be removed from the label as they are not relevant to fumigation of spices.

Other Information

Any person may file a notice of objection[4] regarding this decision on ethylene oxide within 60 days from the date of publication of this Re-evaluation Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides and Pest Management portion of Health Canada's website (Request a Reconsideration of Decision) or contact the PMRA's Pest Management Information Service.

[4] As per subsection 35(1) of the *Pest Control Products Act*.

Appendix I Comments and Responses

1. Comment related to the exposure limit

Stakeholders commented that the proposed 0.1 ppm exposure limit on 8-hour time weighted average (8-hour TWA) is unwarranted, and that reliable detection at this level may not be feasible due to analytical method limitations.

PMRA Response

Taking into consideration that the United States Occupational Safety and Health Administration established the exposure limit for ethylene exposure at 1.0 ppm (8-hour TWA), which is consistent with the recommendations of the American Conference of Industrial Hygienists, the PMRA has revised the exposure limit to 1.0 ppm (8-hour TWA).

2. Comment related to using a tiered data system and additional toxicology studies for ethylene chlorohydrin

Stakeholders requested clarification on what toxicological data was considered as part of ethylene oxide re-evaluation. Stakeholders also commented that a tiered data system should be used for assessing toxicology study requirements, whereby a lack of certain effects in subchronic studies was offered as a rationale for removing the PRVD requirement for additional developmental and reproductive toxicology studies for ethylene chlorohydrin.

PMRA Response

The proposed re-evaluation decision was based on the recent assessments of ethylene oxide from the USEPA Reregistration Eligibility Decision document for ethylene oxide, dated 31 March 2008, and the USEPA Tolerance Reassessment Progress and Risk Management Decision, dated 24 July 2006. The USEPA documents/information can be found on the USEPA Pesticide Registration Status site at http://www.epa.gov/pesticides/reregistration/ethylene_oxide/.

The PMRA does not generally consider a lack of reproductive-related effects in subchronic systemic toxicity studies to be a basis for discounting the need for dedicated developmental and reproductive studies. In the case of the ethylene chlorohydrin review, all relevant potential reproductive and developmental effects could not be accounted for by available subchronic toxicity studies. Therefore, reproductive and developmental toxicity studies are required by the PMRA.

The USEPA considered the short-term toxicology studies on file as acceptable/non-guideline studies. The PMRA has therefore revisited these proposed toxicology study requirements and despite some limitations, the short-term studies are no longer required (see Appendix II). The remaining toxicology studies (chronic, reproductive and developmental studies) are critical for the risk characterization of ethylene chlorohydrin. Therefore, The PMRA maintains the requirement for these toxicological studies.

3. Comment related to air monitoring of the entire facility

Stakeholders commented that the proposed additional requirement on air monitoring data of the entire facility would be very costly and difficult to monitor in many areas (i.e. all office space and break areas). A summary of 2011 air monitoring data of all the main operational areas where ethylene oxide exposure could occur were submitted to the PMRA.

PMRA Response

The submitted data indicated that the average levels of ethylene oxide (8-hour TWA) reading were consistently below 1.0 ppm in all areas being monitored. Therefore, the PMRA considers that this requirement has been satisfied, and air monitoring data (DACO 5.10) are no longer required.

4. Comment on the "Restricted Use" classification for ethylene oxide

A stakeholder commented that the "restricted use" classification for ethylene oxide is not applicable to the currently registered ethylene oxide use.

PMRA Response

The use of ethylene oxide requires that applicators hold an appropriate pesticide applicator certificate or license recognized by the province/territory where the application is to occur. The proposed additional statement under "RESTRCTION CLASSIFICATION" clarifies such restrictions related to the use of ethylene oxide for the fumigation of spices. Therefore, the PMRA maintains the restricted use statement.

5. Comment on the additional requirements for clothing worn by employees

A stakeholder commented that the additional requirements for clothing worn by employees should only be applicable when they come in contact with liquid ethylene oxide. The ethylene oxide fumigation process is mainly conducted via a closed system where employees do not routinely come in direct contact with liquid or vaporized ethylene oxide but rather residual vaporized ethylene oxide which does not contaminate clothing.

PMRA Response

The additional clothing requirements to be added to the PRECAUTIONS are only applicable to workers/handlers who apply ethylene oxide or handle treated spices. This clarification has been added to the label amendment (Appendix III, No. 2).

6. Comment requesting harmonization of the Canadian MRL for ethylene oxide with the current US tolerances

A stakeholder requested that the PMRA harmonizes the MRL for ethylene oxide with the current US tolerance, and requested a clarification of the MRL for ethylene chlorohydrin.

PMRA Response

In general, MRLs are not established during the course of a re-evaluation, and therefore, no modification of the current MRLs are required at this time. However, the registrant is encouraged to submit an application to harmonize MRLs with the USEPA tolerances.

Appendix II Additional Data Requirements

The following data are required as a condition of continued registration under Section 12 of the *Pest Control Products Act*. The registrant of the ethylene oxide product is required to provide these data or an acceptable scientific rationale for a waiver within the timeline specified in the decision letter the PMRA will send.

1) An application to register a technical source for ethylene oxide:

- DACO 2 - Chemistry requirements for the registration of a technical grade active ingredient (TGAI).

2) Toxicology data for ethylene chlorohydrin:

- DACOs 4.4.1 to 4.4.3 - Chronic/Oncogenicity (2 rodent species)
- DACO 4.5.1 - Multi-generation Reproductive Toxicity (rodent)
- DACO 4.5.3 - Developmental Toxicity/Teratogenicity (non-rodent)

These studies must be conducted with the reaction product, ethylene chlorohydrin, which is of suitable quality and purity and be conducted according to the appropriate USEPA Office of Prevention, Pesticides and Toxic Substances or OECD guidelines.

Appendix III Label Amendments for Products Containing Ethylene Oxide

The label amendments presented below do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Information on labels of currently registered products should not be removed unless it contradicts the label statements below.

The labels of end-use products in Canada must be amended to include the following statements to further protect workers and the environment.

1. Restricted Classification

The following statement must be included on the primary display panel of the label:

RESTRICTED PRODUCT

This product is only to be used by individuals holding an appropriate pesticide applicator certificate or license recognized by the provincial/territorial pesticide regulatory agency where the pesticide application is to occur.

2. Label amendments and user safety requirements to further protect people handling ethylene oxide and treated spices

Add to **PRECAUTIONS:**

Wear a long-sleeved shirt, long pants, shoes plus socks, and chemical-resistant gloves during mixing, loading, transfer, application or any other handling activities. A NIOSH/MSHA approved respirator must also be worn under the following conditions:

- when the ambient ethylene oxide concentration is **1 to 50 ppm** – wear a full-facepiece respirator with ethylene oxide approved canister, front or back mounted;
- when the ambient ethylene oxide concentration is **50 to 2,000 ppm** – wear (1) a positive-pressure supplied-air respirator equipped with full-facepiece, hood, or helmet; or (2) a continuous-flow supplied-air respirator (positive-pressure) equipped with hood, helmet, or suit;
- when the ambient ethylene oxide concentration is **greater than 2,000 ppm or unknown** (for example, emergency situations) - wear (1) a positive-pressure self-contained breathing apparatus equipped with full-facepiece; or (2) a positive-pressure full-facepiece supplied-air respirator equipped with an auxiliary positive-pressure self-contained breathing apparatus (SCBA).

The respiratory protection must fit properly, any obstruction to a proper fit should be removed (for example, beard, long sideburns).

When handlers could have eye or skin contact with ethylene oxide or ethylene oxide solutions, such as during maintenance and repair, vessel cleaning, or cleaning up spills, they must wear:

- chemical-resistant attire, such as an apron, protective suit, or footwear that protects the area of the body that might contact ethylene oxide or ethylene oxide solutions, and
  face-sealing goggles, a full face shield, or a full-face NIOSH/MSHA-approved respirator.

Add to **DIRECTIONS FOR USE:**

Fumigation with ethylene oxide must be performed only in vacuum or gas tight chambers designed for use with ethylene oxide.

Safety and awareness training is required for all employees including office staff. Information and training must be provided to all employees in the facility at the time of initial assignment and annually thereafter. The safety training must include, at a minimum, the following information:

- the most recent monitored ambient levels of ethylene oxide in the facility;
- the potential health effects from the levels of ethylene oxide in the facility;
- the emergency response plan and how to respond in an emergency;
- the availability of the Material Safety Data Sheet and other materials related to the health hazards of exposure to ethylene oxide.

In order to reduce ambient levels of ethylene oxide, lengthy facility aeration is encouraged. A reduced ambient level of ethylene oxide greatly reduces potential long-term risks to employees not directly involved in the ethylene oxide applications

DO NOT discharge effluent containing this product into sewer systems, lakes, streams, ponds, estuaries, oceans or other waters.

For fumigation of spices and natural seasonings:

DO NOT use in or on any form of basil.

This product may only be applied to or on whole or ground spices and other processed natural seasonings (except mixtures to which salt has been added) utilizing an ethylene oxide method that uses a single chamber to pre-condition and aerate with an alternating vacuum and aeration purging procedure.

Place spices in the treatment chamber. Assure that the mixture of ethylene oxide and air is compatible with the chamber design, then, introduce into the chamber a concentration of ethylene oxide not to exceed 500 mg/L, with a dwell time not to exceed 6 hours. Then evacuate the gas from the chamber using a sequence of not less than 21 steam washes (injections and evacuations) between 1.5 pounds per square inch absolute (PSIA) (10.34 kPa) and 5.0 PSIA (34.47 kPa) while maintaining a minimum chamber temperature of 46°C.

3. Additional label amendments

Remove statements that refer to American regulations.